Tetrahedron Letters,Vol.26,No.39,pp 4711-4714,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

DIASTEREOSELECTIVITY IN INTRAMOLECULAR ADDITIONS OF ALLYLSILANES TO ENONES

George Majetich*, Jean Defauw, Ken Hull and Thomas Shawe
Department of Chemistry, University of Georgia
Athens, Georgia 30602

SUMMARY: The nature of the catalyst governs the stereochemical outcome in the formation of substituted hydrindanones and related species via intramolecular Sakurai condensations.[1]

The intramolecular Sakurai reaction has recently received considerable attention.[2] We have demonstrated the ability of this annulation procedure to generate bicyclic systems possessing five-, six-, seven-, and eight-membered rings.[3,4] Our study of the stereoselectivity of these processes showed a direct correlation between the catalyst and the stereochemical outcome of cyclizations which result in the creation of three contiguous asymmetric centers of definable relative configuration. These different stereochemical trends (generalized below) can be explained by considering the disposition of the reactive centers prior to carbon-carbon bond formation.

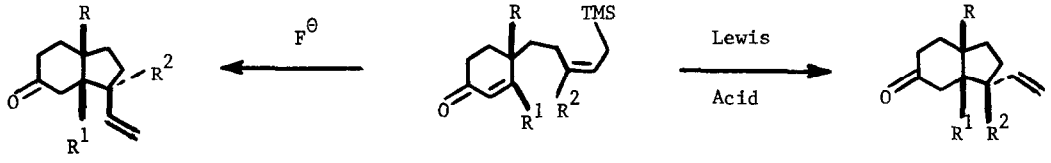


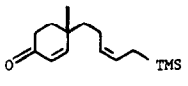
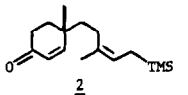
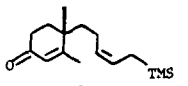
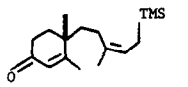
Table I illustrates the contrasting results of the fluoride ion and the Lewis acid-catalyzed cyclizations[5] in the preparation of several substituted hydrindanones.[6,7]

Lewis acid-initiated cyclization via either a synclinal (syn) or antiperiplanar (anti) orientation of the olefinic components permits the stereoelectronically-favored axial approach of the ambident allylic nucleophile, and leads to the expected cis relationship of the R and R1 substitutents (Scheme I). However, the synclinal orientation results in a cis relationship of the substitutents R1 and R2, while an anti orientation leads to a trans configuration of R1 and R2.

In a limited study, Schinzer and co-workers have also reported the Lewis acid-mediated cyclization of substrates **1** and **3**.[2b] Although we concur with their observation that these cyclizations display both a catalyst dependency and a modest temperature effect, we do not favor the intermediacy of a 13-membered ring chelate to account for the preference for a synclinal transition state.[8] Although such a chelate can not be ruled out, this explanation limits the role which the trimethylsilane moiety plays.

We propose that the synclinal orientation permits the developing carbonium ion to be stabilized by the nearby π-electrons of the titanium (or aluminum) enolate, e.g. cationic intermediate "**A**". This π-overlap stabilization is geometrically precluded in cationic intermediate "**B**", which is derived from an anti orientation. Examination of models reveals

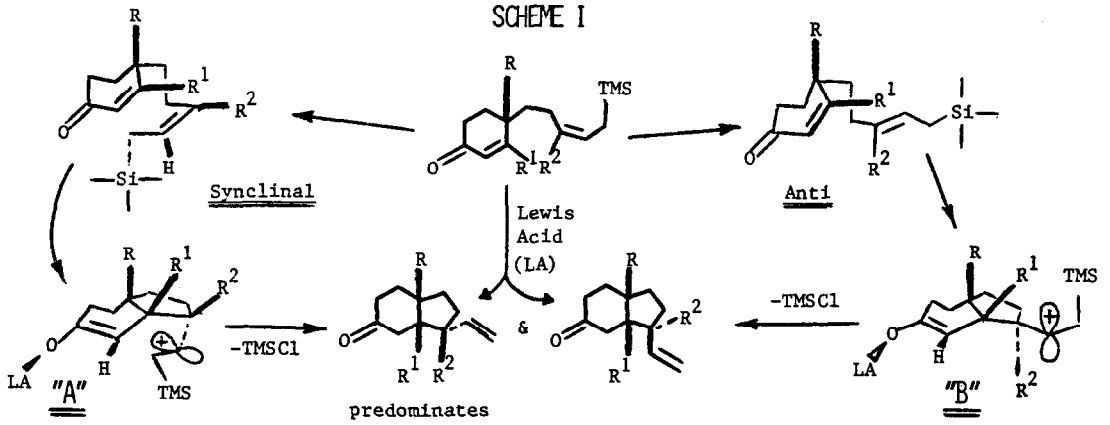
TABLE I

Substrate	CATALYST	Ratio of Isomers		Combined Yield
 1	$F^{\ominus}$	1	1	(77%)
	$EtAlCl_2$	1	3	(62%)
 2	$F^{\ominus}$	4	1	(88%)
	$EtAlCl_2$	1	5	(71%)
 3	$F^{\ominus}$	6	1	(82%)
	$TiCl_4$	1	3+4	(77%)
 4	$F^{\ominus}$	2+3	1	(70%)
	$TiCl_4$	1	4	(78%)

that the introduction of alkyl substituents at either R1 or R2 increases steric congestion in the syn-transition state, cf. enones **2**, **3**, and **4**. Normally such steric interactions would lead to a distinct preference for the anti (less congested) orientation of the double bonds; yet, the predominant products can only be accounted for by a synclinal geometry. Clearly conformational biasing is not the source of stereocontrol. This stereochemical outcome is, however, consistent with a π-overlap stabilization analysis.[9] Santelli's intermolecular allylsilane condensations[10] and Arigoni's stereochemical study of the olefinic cyclization of linalool to terpineol[11] are precedents which support this hypothesis.

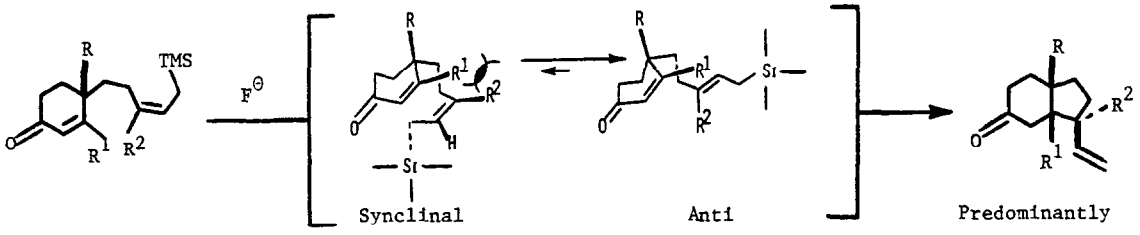
In contrast to the Lewis acid-initiated reactions, the kinetically controlled fluoride ion-induced cyclizations produced hydrindanones in which the anti relationship between the R1 and R2 substituents is preferred. We may also interpret these results in terms of the

SCHEME I



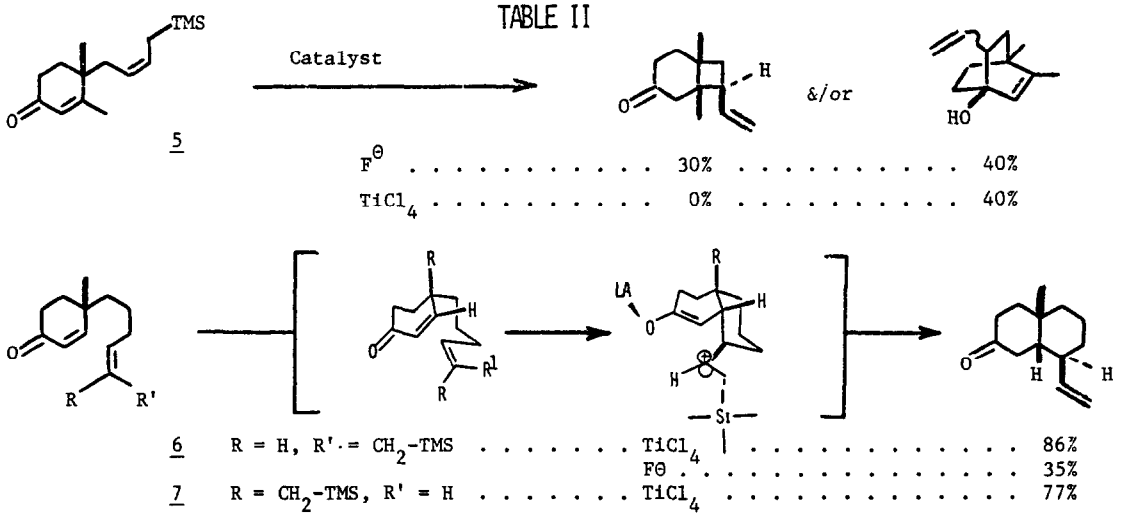
geometries of the olefinic components prior to cyclization (Scheme II). We mentioned that introducing alkyl substituents at either R1 or R2 leads to a decided preference for the anti orientation owing to steric congestion. Indeed, the cyclizations of substrates **2**, **3** and **4** demonstrated considerable stereoselectivity owing to such conformational biasing. Unfortunately, when R1 and R2 are small non-sterically interacting substituents, the stereoselectivity decreases; e.g. **1**.

SCHEME II



Examination of additional cases (Table II) lead to three useful conclusions. First, only a single stereoisomer of the fused bicyclic products was obtained. Second, annulation of a cyclobutane ring justifies our belief that the fluoride-induced cyclizations are kinetically controlled, i.e., the cyclization of substrate **5**. Finally, the Lewis acid-mediated cyclizations of the isomeric allylsilanes **6** and **7** generated identical decalone products.[12] This stereochemical outcome is consistent with the Stork-Eschenmoser Postulate which holds that such cyclizations should occur via a chair-like conformation of the nascent cyclohexane ring, i.e., the transition state shown below.

TABLE II

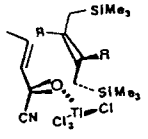


In conclusion, the stereochemical outcome for intramolecular Sakurai reactions is dependent on the choice of catalyst. Our results indicate that the Lewis acid-catalyzed reactions prefer a synclinal orientation of the reactive centers, while fluoride-induced reactions prefer the anti orientation.

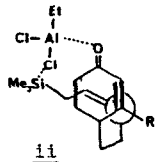
ACKNOWLEDGMENTS: Special thanks are extended to John Wunderlich and George Combs for their help in performing the differential NOE experiments. Substrates **7** was prepared by Jose' Soria.

REFERENCES:

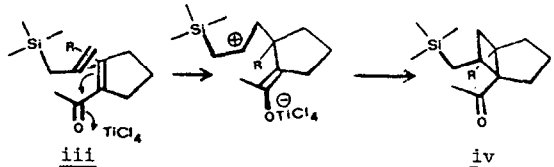
1. This work was presented in part at the 36th Southeast Regional Meeting of the ACS in Raleigh, N.C., October, 1984; Abstract No. ORGN 420, and the 189th National Meeting of the ACS in Miami Beach, April, 1985; Abstract No. ORGN 220.
2. For examples of diastereoselection in intramolecular Hosomi-Sakurai reactions see: a) Schinzer, D. Angew Chem. Int. Ed. Engl. **1984** 23, 308; b) Schinzer, D.; Solyom, S.; Bechker, M. Tetrahedron Lett., **1985**, 26, 1831; c) Tokoroyama, T.; Tsukamoto, M.; Iio, H. Tetrahedron Lett., **1984**, 25, 5067.
3. We have exploited the ability for diastereoselection in intramolecular allylsilane additions in a stereoselective synthesis of (±) nootkatone and (±) valencene: Majetich, G.; Behnke, M.; Hull, K. J. Org. Chem., **1985**, 50, 0000.
4. a) Majetich, G.; Desmond, R.; Casares, A.M. Tetrahedron Lett., **1983**, 24, 1913; b) Majetich, G.; Hull, K.; Defauw, J.; Desmond, R. ibid., **1985**, 26, 2747; c) Majetich, G.; Hull, K.; Desmond, R. ibid., **1985**, 26, 2751; d) Majetich, G.; Hull, K.; Defauw, J.; Shawe, T. ibid., **1985** 26, 2755.
5. In 1978, Sarkar and Andersen first demonstrated the contrasting results of the fluoride versus Lewis acid catalyzed intramolecular allyslilane-aldehyde condensation: Sarkar, T. K.; Andersen, N. H. Tetrahedron Lett., **1978** 3513. Denmark and co-workers have examined the stereochemical outcome of similar cyclizations where the syn and anti orientations are well defined. Their results suggest that reactions catalyzed by Lewis acids favor synclincal transition states, while fluoride induced reactions prefer an anti orientation of the reactive centers: Denmark, S.; Weber, W. Helv. Chim. Acta, **1983**, 66, 1655.
6. a) The spectroscopic data obtained for all new compounds were fully consistent with the assigned structures; b) Reaction conditions have not been optimized; c) All yields are isolated yields; d) The ratios of stereoisomers were based on either NMR integration ratios or isolated material; e) Assignment of the configurations of the products followed from NOE experiments on a JEOL FX270 NMR; f) The preparation of substrates **1**→**4** is discussed in reference 4d.
7. We attempted to prepare the trans isomers of substrates **1** and **3**. In our hands, protodesilylation occurred on all attempts to purify these compounds. This sensitivity contrasts with that of numerous analogs which possess a trans-allylsilane moiety.
8. Santelli and co-workers have invoked a similar (intermolecular) chelation explanation (i) for the intermolecular condensation of (E)-1,4-ditrimethylsilyl-2-butene with α,β-ethylenic acyl cyanides: El-Abed, P.D.; Jellal, A.; Santelli, M. Tetrahedron Lett., **1984**, 25, 1463.
9. Although the 13-membered ring chelate model (ii) would also predict the same preference for syn-transition states in these reactions, this model is not consistent with Kumada's and Fleming's conclusions that electrophilic addition to allylsilanes proceeds via an $SE2'$ process with an anti relationship between the silyl moiety and the double bond: a) Hayashi, T., Kabeta, K.; Hamachi, I.; Kumada, M. Tetrahedron Lett., **1983**, 24, 2865 and references cited therein. b) Fleming, I.; Terrett, N.K., ibid., **1983**, 24, 4153.



i



ii



iii iv

10. The formation of significant quantities of (trimethylsilyl)-methylcyclobutane (**iv**) requires a syn orientation of the allylsilane, which places the carbonium ion (**iii**) close to the titanium enolate so bonding favorably competes with desilylation: Pardo, R.; Zahra, J-P.; Santelli, M.; Tetrahdron Lett., **1979**, 4557. Similiar results were also reported by Sakurai and co-workers: Hosomi, A.; Kobayashi, H.; Sakurai, H. ibid., **1980**, 21, 355.
11. In a study on the stereochemistry of olefinic cyclizations, Arigoni showed that the attacking double bond adopts an orientation in which the π-system stabilizes the developing allylic carbonium ion independent of steric considerations: Godfredsen, S.; Obrechit, J.P.; Arigoni, D. Chimia, **1977**, 31, 62.
12. Earlier this year,[4d] we reported that the cyclization of substrate **6** failed using fluoride catalysis. Re-investigation of this reaction afforded the decalone shown (35%).

(Received in USA 17 June 1985)